Robust Summaries

Monoglyme

Physicochemical Properties

Melting Point

Type Melting Point

Test Substance 1,2-Dimethoxyethane
CAS Number: 110-71-4

Method

- Guideline: None
- Test Type: Melting Point
- GLP: No
- Year: Unknown

Result

- Melting Point: -58 deg C

Remarks Field for Results: Handbook data

Conclusions

Remarks Field: The melting point is –58˚C

Data Quality

- Reliability: Klimisch Code 2. A reliability code of 2 is assigned to data from reference handbooks.

References

1. Lide, D.R. (ed). CRC Handbook of Chemistry and Physics. 76ed ed. Boca Raton, FL: CRC Press, 1995-1996, page 3-154.
2. Budavari, S. (ed.). The Merck Index Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989. 509.

Other

Boiling Point

Type	Boiling Point
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4

Method

• Guideline	None
• Test Type	Boiling Point
• GLP	No
• Year	Unknown

Result

• Boiling Point	85 deg C @ 760 mm Hg (1) 82-83 deg C @ 760 mm Hg (2)
Remarks Field for Results	Handbook data

Conclusions

Remarks Field	Boiling point is between 82 and 85 deg C @ 760 mm Hg

Data Quality

• Reliability	Klimisch Code 2. A reliability code of 2 is assigned to data from reference handbooks.

References

1. Lide, D.R. (ed). CRC Handbook of Chemistry and Physics. 76ed Boca Raton, FL: CRC Press, 1995-1996, page 3-154.
2. Budavari, S. (ed.). The Merck Index Encyclopedia of Chemicals, Drugs and Biologicals. Rahway, NJ: Merck and Co., Inc., 1989. 509.

Other

Vapor Pressure

Type	Vapor Pressure
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4

Method

• Guideline	None
• Test Type	Vapor Pressure
• GLP	No
• Year	Unknown

Result

• Vapor Pressure	48 mm Hg @ 20 Deg C (1)
Remarks Field for Results	Handbook data

Conclusions

Remarks Field	Vapor pressure is 48 mm Hg at 20˚C

Data Quality

• Reliability	Klimisch Code 2. A reliability code of 2 is assigned to data from reference handbooks.

References

1. Riddick, J.A., W.B. Bunger, Sakano T.K. Techniques of Chemistry 4th ed., Volume II. Organic Solvents. New York, NY: John Wiley and Sons., 1985. 296

Other

Partition Coefficient, Octanol-Water

Type	Partition Coefficient, Octanol-Water
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4

Method

• Guideline	Not specified
• Test Type	Partition Coefficient, Octanol-Water
• GLP	No
• Year	1995

Result

• Log $k_{o/w}$	Experimental	-0.21 (1)
	Calculated by KOWWIN	-0.21(2)

Remarks Field for Results: 1,2-Dimethoxyethane was one of the reference compounds for development of the KOWWIN program (module of EPIWIN). The experimental value is from the literature. The calculated value is the result of the KOWWIN calculation.

Conclusions

Remarks Field: The log $K_{o/w}$ is approximately –0.21. This material is expected to be relatively water soluble and not bioaccumulate to any significant degree.

Data Quality

• Reliability: Klimisch Code 2. A reliability code of 2 is generally assigned to literature values not conducted under OECD guidelines or glps.

References

1. Hansch. C., A. Leo and D. Hoekman. Exploring QSAR. Hydrophobic, Electronic, and Steric Constants. ACS Professional Reference Book. Wshington, DC: American Chemical Society. 1995.
2. KOWWIN v 1.66, Syracuse Research Corporation, Syracuse, NY (April 2000)

Other

Water Solubility

Type	Water Solubility
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4

Method

• Guideline	None specified
• Test Type	Water Solubility
• GLP	No
• Year	Unknown

Result

• Solubility	Soluble in water in all proportions.
Remarks Field for Results	Handbook data

Conclusions

Remarks Field	Material is soluble in water in all proportions.

Data Quality

• Reliability	Klimisch Code 2. A reliability code of 2 is assigned to data from reference handbooks.

References

1. Merck Index, 9th Edition, Merck Inc, Rahway NJ p1249 (1976)

Other

Fate

Photodegradation

Type Photodegradation

Test Substance 1,2-Dimethoxyethane
CAS Number: 110-71-4

Method

- Guideline: Estimated Using version 1.90 of the Atmospheric Oxidation Program for Microsoft Windows (AOPWIN)[1] which estimates the rate constant for the atmospheric, gas-phase reaction between photochemically produced hydroxyl radicals and organic chemicals. The rate constants estimated by the program are then used to calculate atmospheric half-lives for organic compounds based upon average atmospheric concentrations of hydroxyl radical.
- Test Type: Photodegradation Estimate
- GLP: No
- Year: 2001

Results

- Result: APOWIN estimated OH rate constant 15.7×10^{-12} cm^3/molecule-sec

Remarks Field for Results: The APOWIN estimate for the reaction rate is based on simple hydrogen abstraction. Similar compounds provide estimates close to measured values for this rate constant. Thus, the method is expected to provide an accurate estimate of the reaction rate constant with hydroxyl radical. Based on the estimated rate constant and using the defaults in APOWIN (1,500,000 OH radicals/cc and a 12-hour day) for atmospheric hydroxyl radical concentration, the estimated half-life is approximately 8.2 hours.

Conclusions

Remarks Field: The atmospheric half-life of 1,2 Dimethoxyethane in the atmosphere is estimated to be in the range of 8.2 hours

Data Quality

- Reliability: Klimisch Code 2. A reliability code of 2 is assigned a result using an accepted method of estimation.

References

1. Syracuse Research Corporation, Syracuse, NY (April 2000)

Other

Water Stability

Type	Water Stability
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4

Method

• Guideline	None
• Test Type	Hydrolysis as a Function of pH
• GLP	No
• Year	2001
Remarks Field for Test Conditions	This material has no groups that are susceptible to hydrolysis in the pH 4 to 9 range (see reference); therefore, it is considered stable to hydrolysis in surface and groundwater. It is estimated to have a hydrolysis half-life of greater than one year between pH 4 and pH 9. The estimation program in EPIWIN has no capability to estimate hydrolysis rates of ethers (1).

Results

•	Material is considered stable in water
• Percent Degradation	Negligible
• Breakdown Products	None

Conclusions

Remarks field	Actual experience in use of this material as a process aid and component of aqueous solutions confirms the stability in water.

Data Quality

• Reliability	Klimisch Code 2. A reliability code of 2 is assigned to values obtained from reliable estimation methods.

Reference

Lyman, W. J. et al. (1990). Handbook of Chemical Property Estimation Methods, pp. 7-4, Amer. Chem. Society, Washington, DC

Other

Reference for supporting study

1. HYDROWIN modeling program, version 1.67, as found in EPIWIN v 3.05, Syracuse Research Corporation, Syracuse NY (April 2000).

Theoretical Distribution (Fugacity)

Type	Theoretical Distribution (Fugacity)
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4

Method

- Guideline: Estimated using the Mackay model with standard defaults contained in EPIWIN v 3.05.[1]
- Test Type: Level III Fugacity Model
- GLP: No
- Year: 2001

Remarks Field for Method

```
Inputs for the model were adjusted to match the measured values of
known parameters. Biodegradation parameters were estimated from
the literature. Equal quantities were assumed to initially be
distributed to air, water and soil. The inputs and full output of
the EQC Level III model are below:

Level III Fugacity Model (Full-Output):
=======================================
  Chem Name   :     Monoglyme
  Molecular Wt:     90.12
  Henry's LC  :     1.07e-006 atm-m3/mole (Henrywin program)
  Vapor Press :     48 mm Hg  (user-entered)
  Log Kow     :     -0.21  (user-entered)
  Soil Koc    :     0.253  (calc by model)

          Concentration   Half-Life    Emissions
            (percent)        (hr)       (kg/hr)
   Air       0.951           17           1000
   Water     61              3e+003       1000
   Soil      38              3e+003       1000
   Sediment  0.116           6e+003       0

     Fugacity    Reaction    Advection   Reaction    Advection
       (atm)      (kg/hr)      (kg/hr)    (percent)   (percent)
 Air    5.85e-011    880          216         29.3      7.2
 Water  8.22e-011    320          1.38e+003   10.7      46.1
 Soil   1.86e-009    199          0           6.64       0
 Sed    7.8e-011     0.305        0.0528      0.0102   0.00176

   Persistence Time: 757 hr
   Reaction Time:    1.62e+003 hr
   Advection Time:   1.42e+003 hr
   Percent Reacted:  46.7
   Percent Advected: 53.3

   Half-Lives (hr), (based upon user-entry):
      Air:      17
      Water:    3000
      Soil:     3000
      Sediment: 6000

   Advection Times (hr):
      Air:      100
      Water:    1000
      Sediment: 5e+004
```

Result

- Distribution
  - Air 0.91 %
  - Water 61 %
  - Soil 38 %
  - Sediment 0.1 %

Remarks Field for Results: This is the currently accepted model for theoretical distribution estimation.

Conclusions

Remarks Field	This material is expected to environmentally distribute primarily in water and soil.

Data Quality

● Reliability	Klimisch Code 2. A reliability code of 2 is assigned a result using an accepted method of estimation.

References

1. Syracuse Research Corporation, Syracuse, NY (April 2000)

Other

Biodegradation

Type	**Biodegradation**
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4
Method	
• Guideline	None
• Test Type	Biodegradation
• GLP	No
• Year	1999
• Contact Time	Varies – days to months
• Inoculum	Acclimated bacteria for a refinery waste-treatment facility.

Remarks for Test Conditions

◊ Innoculum	• The inoculum was obtained initially from a petroleum refinery waste-treatment plant. It was initially seeded in a Submerged Attached Growth Air Lift (SAGAL) reactor where it was in contact with nutrients and a mixture of 10 glycol ethers (including 1,2-dimethoxyethane) for a period of 52 weeks. The batch test on individual glycol ethers we conducted with a high concentration of washed cells from the reactor. • Acclimated to a mixture of glycol ethers
◊ Test Material Concentration	• Initial 600 mg/L as COD
◊ Reference Material	• Ethylene glycol monophenyl ether @ 37 mg/l as COD • Reference material showed 94.4% removal of COD
◊ Incubation Temperature	• 30˚ C
◊ Sampling Frequency	• Not stated • Duplicate bottles sampled
◊ Analytical Method	• COD
◊ Controls and Blanks	• Blank composition not stated • Positive control using Ethylene glycol monophenyl

Result

- Degradation Percent after time: 10.7 % Removal as COD, time not stated
- Result: Recalcitrant to biodegradation
- Kinetics: Not applicable
- Breakdown Products: None determined

Remarks Field for Results: Not readily biodegradable
Duplicate results were 0.7% and 20.7% removal.

Additional studies were conducted by feeding the Submerged Attached Growth Air Lift reactor a mixture of 10 to 40 mg dimethoxyethane as part of a mixture of 10 glycol ethers. Under these conditions, test substance was found to disappear. This was latter attributed to evaporation. After the submerged reactor portion of the study, individual sealed enrichment cultures of each glycol ether were prepared for kinetic determination. In this study, with incubation up to 33 weeks, no loss of test substance was observed. This was quantitatively confirmed using the individual culture described above.

Conclusions

Remarks Field: Not biodegradable under these conditions. Biodegradable glycol ethers found to generally have a free hydroxy group.

Data Quality

- Reliability: Klimisch Code 2. Published report with sufficient detail and controls to provide valuable information.

References

Cowan, R. and Kwon J. Aerobic biodegradation of ethylene glycol ethers. Hazard. Ind. Wastes (1999), 31st, 273-282.

Other

This study is supported by earlier publications that reported 1,2-dimethoxyethane was recalcitrant to biodegradation, has questionable biodegradation, or is not taken up by bacteria.[1,2,3]

The BIOWIN V4.0 model found in EPIWIN gives mixed results with about half the models predicting rapid biodegradation and have predicting slow degradation.[4]

The related compound diglyme is also know to be relatively resistant to biodegradation.[5]

References for Supporting Studies

1. Babeu, L and D D Vaishnav Prediction of biodegradability for selected chemicals. J. Indust. Microbiol. 2:107-15 (1987)
2. Bridie, A, Wolff, C and M Winter. BOD and COD of some petrochemicals. Water Research 10:231-35 (1979).
3. Kawai, F. Bacterial degradation of glycol ethers. Appl. Microbiol. Biotech. 44:532-38 (1995)
4. EPIWIN v 3.05, Syracuse Research Corporation, Syracuse NY (April 2000).
5. Anonymous. TA:Beratergremium fuer umweltrelevante Altstoffe (BUA) PG:70 p YR:1993 IP: VI:67

Effects on Environmental Organisms

Acute Toxicity to Fish

Type	**Acute Toxicity to Fish**
Test Substance	Surrogate 1,2-Diethoxyethane CAS Number: 60-29-7 Purity not specified

Method

• Guideline	None
• Test Type	Acute Toxicity to Fish
• GLP	No
• Year	1977
• Analytical Monitoring	None
• Species/Strain	Lepomis macrochirus Bluegill
• Test Details	Static
• Exposure Period	96 hours
• Statistical Methods	
Remarks Field for Test Conditions	The test conditions varied from study to study. The weight of data indicating low hazard provided by several independent laboratories for this surrogate and this class of chemicals strengthens the conclusion that test conditions were adequate.

Results

• Units	mg./l.
• LC_{50}	> 10,000 (96 hour)
• LC_0	

Remarks Field for Results

Other Supporting Information

◊ Oryzias latipes Medaka	48-Hour LC50 >10,000 mg/L[1]
◊ Pimephales promelas Fathead minnow	96-Hour LC50 = 2560[2]
◊ EPA ECOSAR Model	96-Hour Fish LC50 = 7984 mg/L[3]
◊	

Conclusions

Remarks field

◊ Although no studies have been conducted on this compound, this class of chemicals has been well characterized as having low aquatic toxicity. Also in support of this are data demonstrating low aquatic hazard for the initial metabolite ethylene glycol monomethly ether, which has an LC50 (or EC50) exceeding 10,000 ml/L in bluegill, carp, inland silverside, rainbow trout, daphnia magna and green algae (EPA ECOTOX Data Base). The other initial hydrolytic metabolite methanol has a similar established low aquatic hazard for fish, invertebrates and aquatic plants (see EPA ECOTOX Data Base)

Data Quality

- Reliability

Klimisch Code 2. Reliable estimate based on established methods and validated model.

References

Dawson, G.W., A.L. Jennings, D. Drozdowski, and E. Rider, The Acute Toxicity of 47 Industrial Chemicals to Fresh and Saltwater Fishes. J.Hazard.Mater. 1(4):303-318 (1977) as cited in EPA ECOTOX data-base

Other

Additional support comes from a study of diglyme in which the 96-hour LC0 for the golden orfe (Leuciscus idus) was experimentally determined to be > 2000 mg/l.[4]

References for supporting studies

1. Tsuji, S., Y. Tonogai, Y. Ito, and S. Kanoh . The Influence of Rearing Temperatures on the Toxicity of Various Environmental Pollutants for Killifish (Oryzias latipes). J.Hyg.Chem./Eisei Kagaku 32(1):46-53 (1986) as cited in EPA ECOTOX data-base
2. Geiger, D.L., S.H. Poirier, L.T. Brooke, and D.J. Call. Acute Toxicities of Organic Chemicals to Fathead Minnows (Pimephales promelas), Vol. 3. Center for Lake Superior Environmental Studies, University of Wisconsin, Superior, W I:328 (1986) as cited in EPA ECOTOX data-base
3. ECOSAR modeling program, version 0.99f, as found in EPIWIN v 3.05, Syracuse Research Corporation, Syracuse NY (April 2000). Based on neutral organics model.
4. Anonymous. TA:Beratergremium fuer umweltrelevante Altstoffe (BUA) PG:70 p YR:1993 IP: VI:67

Acute Toxicity to Aquatic Invertebrates

Type	**Acute Toxicity to Aquatic Invertebrates**
Test Substance	Surrogate 2-Methoxy ethanol CAS Number: 109-86-4 Purity not specified

Method

• Guideline	Not specified, published study.
• Test Type	Daphnia, acute immobilization
• GLP	No
• Year	1977
• Analytical Procedures	No data
• Species/Strain	*Daphnia magna*
• Test Details	Static
• Statistical Methods	
Remarks Field for Test Conditions	The test conditions varied from study to study. The weight of data indicating low hazard provided by several independent laboratories for this class of chemicals strengthens the conclusion that test conditions were adequate.

Results

• Nominal Concentrations	
• Units	mg./L.
• EC_{50}	> 10,000 at 24-hours
• EC_0	
Remarks Field for Results	Other Supporting Information

◊	Artemia salina Brine shrimp	24-Hour LC50 >10,000 mg/L[1]
◊	EPA ECOSAR Model	48-Hour daphnid EC50 = 7344 mg/L[2]

Conclusions

Remarks field

Although no studies have been conducted on this compound, this class of chemicals has been well characterized as having low aquatic toxicity. Also in support of this are data demonstrating low aquatic hazard for the initial metabolite ethylene glycol monomethly ether, which has an LC50 (or EC50) exceeding 10,000 ml/L in bluegill, carp, inland silverside, rainbow trout, daphnia magna and green algae (EPA ECOTOX Data Base). The other initial hydrolytic metabolite methanol has a similar established low aquatic hazard for fish, invertebrates and aquatic plants (see EPA ECOTOX Data Base). The 1,2-diethoxy ethane also demonstrates low aquatic toxicity but has not been tested for mortality with daphnids. (see EPA ECOTOX data base).

The EC_{50} (48 hour) of dimethoxyethane is considered to be greater than 1,000 mg/l under these conditions.

Data Quality

- Reliability

Klimisch Code 2 Reliable estimate based on established methods and validated model.

References

Bringmann, G., and R. Kuhn. The Effects of Water Pollutants on Daphnia magna. Z.Wasser-Abwasser-Forsch.10(5):161-166 (GER) (ENG ABS); TR-79-1204, (1977) English Translation, Literature Research Company:13 p. as cited in EPA ECOTOX data-base

Other

References for supporting studies

2. Price, K.S., G.T. Waggy, and R.A. Conway. Brine Shrimp Bioassay and Seawater BOD of Petrochemicals. J.Water Pollut.Control Fed. 46(1):63-77 (1974). As cited in EPA ECOTOX data base.
3. ECOSAR modeling program, version 0.99f, as found in EPIWIN v 3.05, Syracuse Research Corporation, Syracuse NY (April 2000). Based on neutral organics model.

Toxicity to Aquatic Plants

Type Toxicity to Aquatic Plants

Test Substance 1,2-Dimethoxyethane
CAS Number: 110-71-4

Method

- Guideline: Estimated using version 0.99f of the ESCOSAR Program for Microsoft Windows (1) that estimates the aquatic toxicity of a material based on its chemical classification and physico-chemical properties.
- Test Type: Algae inhibition estimate
- GLP: No
- Year: 2001

Remarks Field for Method: The SAR relationship developed for the neutral organics class of compounds toward algae is:

Log 96-h EC50 = 1.466 - 0.885 log Kow

Where the EC50 is in millimoles per liter (mM/L)

The estimated EC_{50} was calculated based on the literature value for the Ko/w and the above equation. As "neutral organics" is a large class of compounds, validation for a related compound with reliable algae data is desirable.

The compounds in the following table were considered similar in regard to potential for algae toxicity.

	Monoglyme	1,3-Dioxolane	1,4-Dioxane	EGMME (a)
Ko/w	-0.21	-0.37	-0.27	-0.77
Water Sol	Misc	Misc	Misc	Misc
VP	48	70	37	9.5
IC50	???	>877(b)	5600 (c)	> 1000 (d)
ECOSAR Prediction	4042	4604	4466	14,200

a. Ethylene glycol monomethyl ether
b. Measured value in OECD 201 study
c. Abstract of BUA Document for 1,4-Dioxane.
d. Abstract of BUA Document for 1,4-Dioxane

Of these three model compounds, 1,3-Dioxolane has reliable data available that can be provided in a robust summary. That summary follows. The 1,3-Dioxolane maximum mean concentration in the algae study was limited by its volatility from water.

Results

- Result — Estimated EC_{50} 4043 mg/L

Remarks Field for Results: The ECOSAR estimate for green algae growth inhibition was validated for this type of material based on a recent study of 1,3-Dioxolane and literature values for 1,4-Dioxane and ethylene glycol monomethyl ether. Although determination of the actual value for the EC50 of 1,3-Dioxolane was complicated by higher volatility than predicted for Monoglyme, this result and the literature values for similar materials indicate the model is valid and there is little environmental hazard to green algae from Monoglyme.

Conclusions

Remarks Field: Based on the validated ECOSAR estimate, this material has low potential for inhibition of algal growth in the environment.

Data Quality

- Reliability: Klimisch Code 2. A reliability code of 2 is assigned a result using an accepted method of estimation.

References

2. Syracuse Research Corporation, Syracuse, NY (April 2001) ECOSAR modeling program, version 0.99f, as found in EPIWIN v 3.05

Other

Toxicity to Aquatic Plants (model validation study)

Type: Toxicity to Aquatic Plants (model validation for ECOSAR estimate)

Alternate Test Material: Surrogate
1,3-Dioxolane
CAS Number: 646-06-0
Purity 99.98%

Represented Material: 1,2-Dimethoxyethane
CAS Number: 110-71-4

Method

- Guideline: OECD 201
- Test Type: Algae Growth Inhibition
- GLP: Yes
- Year: 2000
- Species/Strain: *Selenastrum capricornutum* The culture originated from an inoculum received from the Carolina Biological Supply Company (Burlington, NC) and has been maintained in the laboratory since December 3, 1999.
- Element Basis: Number of cells per ml. And area under the growth curve
- Exposure Period: 72 hours
- Analytical Monitoring: Yes
- Statistical Methods:
  - ◊ EC_{50} values were calculated based on both biomass growth (comparison of area under the growth curves), the E_bC_{50}, and on the average specific growth rate, the E_rC_{50}. EC_{50} values and their 95 percent confidence limits were estimated by a computer program (U.S. EPA, 1994) for calculating EC values by probit analysis.
  - ◊ In addition to the EC_{50} values, a no-observed-effect concentration (NOEC) was calculated by analysis of variance (ANOVA) with statistical differences between cell density means determined by Dunnett's procedure (U.S.EPA, 1988). Statistical differences were determined at a probability level of 0.05.
  - ◊ Inhibition calculations are based upon a comparison of the areas under the growth curves and are reported using the symbol E_bC_{50}. The 24, 48 and 72-hour E_bC_{50} values and their 95 percent confidence limits were calculated.

Remarks Field for Test Conditions

- ◊ Test Temperature Range: The temperature ranged from 24.4 to 26.8º C.

◊ Growth Medium Chemistry

The base water for the test medium was deionized water. The base water was enhanced with reagent-grade nutrients as described in ASTM (1994). The pH of the test medium was adjusted to 7.5 ± 0.1 prior to the addition of the test substance.

[American Society for Testing and Materials (ASTM). 1990. Standard Guide for Conducting Static 96-Hour Toxicity Tests with Microalgae. ASTM Designation E1218-90.]

◊ Dilution Water Source

Deionized water from the Town of Jupiter Florida, supplemented as above.

◊ Exposure Vessel

Sterile 250-mL glass Erlenmeyer flasks covered with gas exchange caps containing 100 ml of algal medium.

◊ Stock Solutions Prepared

Approximately 1.0182 g of the chemical was brought to volume in a 100 ml volumetric flask with deionized water to prepare a stock concentration of 10,200 mg/L. The following amounts of stock (1.9, 3.75, 7.5, 15 and 30 ml) were used to make the test concentrations by mixing with 298.1, 296, 292.5, 285, and 270 ml of freshwater algal media individually.

◊ Light Level and Quality

Lighting was continuous fluorescent lighting and intensity was measured daily at the surface of the test solutions during the 72-hour exposure period and ranged from 84 to 138 $\mu E/m^2/s$ as measured by a LI-COR, Inc. Model LI-189 light meter equipped with a 2π quantum sensor.

◊ Test Design

Replicates: three replicates for each test concentration. Six replicates were used for the dilution water control.

Concentrations were determined by gc using a glp validated method.

- Target: 0, 62.5, 125, 250, 500 and 1000 mg/L
- Mean measured Control (<31.0) , 36.9, 81.0, 163, 280 and 877 mg/L.

◊ Analytical Determination of Test Material Concentrations

	Measured Concentrations mg/L			
Nominal Conc	Day-1	Day-3	Mean	Percent nominal

Concentrations

Control	ND	ND	---	---
62.5	60.6	13.1	36.9	59
125	124	37.9	81	64.8
250	262	64.7	163	65.2
500	520	39.3	280	56
1000	1027	726	877	87.7

◊ Method of calculating mean: Arithmetic based on composite samples of each replicate for each concentration at study initiation and study termination

◊ Exposure period: 72 hours

◊ Cell Counts: Algal growth was measured by direct cell count using a 0.1mm deep hemacytometer under a compound microscope. Algal counts were conducted on day one and approximately every 24 hours thereafter. Morphological observations were also conducted on the test treatment using a compound microscope to detect abnormal cell morphology and coloration as compared to the control replicates.

Results

- Nominal Concentrations: 0, 62.5, 125, 250, 500 and 1000 mg/L
- Measured Concentrations: (<31.0), 36.9, 81.0, 163, 280 and 877 mg/L
- Units: mg./L
- EC_{50}: The E_bC_{50} and E_rC_{50} (0-72 hours) were >877 mg /L.
- NOEC: 877 mg/L (72-hour)

Remarks Field for Results

◊ Biological Observations

After 72 hours of exposure to 1,3-Dioxolane, the percentage cell growth inhibition (based on area under the growth curve) compared to the control was 19% at the mean measured concentration of 877 mg/L. The growth curves of both the control and the test solution exhibited a pattern of exponential growth during the 72-hour growth period. Observations of cell morphology detected no changes in exposed cells as compared to cells in the control media. There was no significant statistical difference between the algal growth of the control and the test solutions

◊ Daily Cell Counts From Each Replicate

These are presented to substantiate that there was no unusual variation between replicates associated with the possible selective volatilization of the test material from individual flasks.

Measured Conc (mg/L)	Cell Numbers (x 10^4)/ml			
	Replicate	24 hrs	48 hrs	72 hrs
Control	A	1.7	25	407
	B	2.1	36	378
	C	1.1	33	280
	D	0.9	43	358
	E	1.8	28	224
	F	1.9	26	289
36.9	A	1.3	13	318
	B	1.3	23	284
	C	2.2	16	218
81	A	1.9	33	329
	B	1.6	20	298
	C	0.9	48	333
163	A	0.4	30	304
	B	0.9	30	336
	C	1.8	56	189
280	A	1.7	29	324
	B	2.0	24	278
	C	1.3	40	291
877	A	2.1	33	229
	B	3.3	37	287
	C	2.1	34	211

◊ Mean Cell Density at Each Concentration at Each Time Point

Measured Conc (mg/L)	Mean Cell Numbers (x 10^4)/ml (s.d.)		
	24 hours	48 hours	72 hours
Control	1.6 (0.475)	32 (6.91)	323 (69.4)
36.9	1.6 (0.520)	17 (5.13)	273 (50.8)
81	1.5 (0.513)	34 (14.0)	320 (19.2)
163	1.0 (0.709)	39 (15.0)	276 (77.3)
280	1.7 (0.351)	31 (8.18)	298 (23.7)
877	2.5 (0.693)	35 (2.08)	242 (39.7)

◊ Percent Inhibition

Measured Conc (mg/L)	Percent Inhibition		
	0-24hrs	24-48 hrs	48-72 hrs
36.9	0	-47	-21
81	-17	6	0
163	-100	18	-9
280	17	-2	-7
877	150	15	-19

Conclusions

Remarks Field

The E_bC_{50} and E_rC_{50} (0-72 hours) were >877 mg /l (based on measured concentrations). The 72-hour no-observable-effect concentration (NOEC) was 877 mg/L.

The test material was somewhat volatile; however, sufficient Dioxolane remained in the culture flasks (especially at the highest concentration tested) to provide a valid estimate of the growth inhibition potential of the test material to green algae.

Data Quality

- Reliability

Klimisch Code 1. Reliable without restriction. Study was conducted in accord with current OECD guideline under glp conditions. Analytical measurements verified exposure concentrations.

References

1,3-Dioxolane: Toxicity to The Freshwater Green Alga, *Selenastrum capricornutum*, Under Static Test Conditions. Toxikon Laboratories, Jupiter FL, Project ID 00J0009b, 27 September 2000, submitted to and sponsored by Ticona Corporation and Ferro Corporation.

Other

This study is supported by an earlier study, sponsored by Celanese, in which Trioxane was tested for growth inhibition of *Selenastrum capricornutum*. In this study, algae growth was measured out to 14 days of exposure at levels of 1000, 5000 or 10000 mg/L with counts recorded on days 3, 6, 10 and 14. Significant inhibition was seen only at 5000 mg/L and above 1000 mg/L was determined to be the NOEC. Graphically, the 96-hour EC_{50} can be determined to be in the range of 4000 mg/L; however, loss of test material may affect this estimate[1]

The EPA ECOSAR Modeling Program found in EPIWIN, estimates the 96-hour EC_{50} for green algae to be 4075 mg/L.[2]

References for supporting studies

1. Report to Celanese Chemical Company Inc. on Toxicology and Fate of Selected Industrial Chemicals in Aquatic Ecosystems. J.R. Walton and E.M. Davis, University of Texas at Houston. December 1980.
2. ECOSAR modeling program, version 0.99f, as found in EPIWIN v 3.05, Syracuse Research Corporation, Syracuse NY (April 2000).

Acute Health Effects

Acute Oral Toxicity

Type	**Acute Oral Toxicity**
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4 (Aldrich Chemical Company)

Method

- Guideline: None specified
- GLP: No
- Year: 1983
- Species: Rat
- Strain: Unspecified
- Route of administration: Oral Gavage
- Doses: 500, 1000, 2000 and 4000 mg/kg
- Sex: Female
- Number of Animals/group: Four
- Vehicle: None noted

Remarks Field for Test Conditions	◊ Age at Study Initiation	Unknown
	◊ Doses	500, 1000, 2000 and 4000 mg/kg
	◊ Volume administered	Not specified
	◊ Post-dose observation period	14 Days
	◊ Other	

Results

- LD_{50} >4000 mg/kg
- Number of deaths at each dose level

Dose	Mortality
500 mg/kg	0/4
1000 mg/kg	1/4
2000 mg/kg	0/4
4000 mg/kg	1/4

Remarks Field for Results

◊ Time of death	Not stated
◊ Clinical Signs	Rats at 2000 and 4000 mg/kg were unbalanced and lethargic after treatment.
◊ Body Weights	All surviving animals gained weight during the two-week observation period
◊ Necropsy Findings	None
◊ Target Organs	None identified

Conclusions

Remarks field: Study documentation available is minimal. Results are consistent with other data for the material. The study appears to have been well conducted by a respected laboratory.

Data Quality

- Reliability: Klimisch Code 2. Study design, conduct and reporting are considered reliable to address the test endpoint although not conducted in accord with GLP standards.

References

Acute Toxicological Properties and Industrial Handling Hazards of 1,2-Dimethoxyethane. Dow Chemical USA, R&D Report August 25, 1983. TSCA Initial Submission (Final Report) With Cover Letter Dated 051492. NTIS/OTS0539769

Other

This study is supported by a letter report from Kodak to DuPont, dated March 20,1979, in which acute toxicity information is given. The acute oral information is in accord with the information in this Robust Summary. The information provided by Kodak is given in the table below. (1)

Route or Target Organ	**Result**
Oral LD_{50} rat	>3200 mg/kg
Oral LD_{50} mouse	Approximately 3200 mg/kg
Intraperitoneal LD_{50} rat	800 mg/kg
Intraperitoneal LD_{50} mouse	400-800 mg/kg
Inhalation rat LD_{50} (6 hour)	Between 20 and 63 mg/L
Dermal LD_{50} guinea pig	5-10 mg/kg (with mod skin irritation)
Eye Irritation (rabbit)	Slight irritation

References for supporting studies

1. Initial Submission: Letter From Dupont Chem To USEPA Regarding Toxicity Studies Of 1,2-Dimethoxyethane With Cover Letter Dated 10-15-92. EPA/OTS; Doc #88-920009666 NTIS/OTS0571323

Acute Inhalation Toxicity

Type	**Acute Inhalation Toxicity**
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4
Method	
• Guideline	None specified
• GLP	No
• Year	1979 or earlier
• Species	Rat
• Strain	Not specified
• Route of administration	Whole-body inhalation as vapor
• Doses	20 or 63 mg/L
• Sex	Not specified
• Exposure Period	Six hours
• Number of Animals/group	Not specified
• Vehicle	Air
Remarks Field for Test Conditions	◊ Age at Study Initiation: Not specified ◊ Doses: 20 or 63 mg/L ◊ Post-dose observation period: 14 Days
Results	
• LC_{50}	>20 mg/L
• Number of deaths at each dose level	◊ 20 mg/L 0% ◊ 63 mg/L 100% (All survived exposure but died within 72 hours)

Remarks Field for Results	Clinical Signs	
	20 mg/L	Exposure to 20 mg/Liter for six hours produced only signs of irritation and slight ataxia. None of the animals died and all gained weight normally in the 14- day observation period following exposure.
	63 mg/L	Rats exposed to calculated vapor concentration of 63 mg/L showed signs of irritation at the beginning of exposure. This progressed to prostration after approximately 1 1/2 hours and they remained prostrate until the six-hour exposure was terminated. Although all of the animals survived the exposure, all of them died within 72 hours post-exposure.

Conclusions

Remarks field

The six-hour inhalation LC_{50} is between 20 and 63 mg/L. The vapors produced some irritation and anesthesia at the high level.

Data Quality

- Reliability

Klimisch Code 2. Study results are considered reliable to address the test endpoint in consideration of supporting data available from other studies.

References

Letter report from Kodak to DuPont, dated March 20,1979. Initial Submission: Letter From Dupont Chem To USEPA Regarding Toxicity Studies Of 1,2-Dimethoxyethane With Cover Letter Dated 10-15-92. EPA/OTS; Doc #88-920009666 NTIS/OTS0571323

Other

This study is supported by a letter report from Dow Chemical company dated August 25, 1983 in which is was reported that a group of 4 female rats was exposed to vapor of test material calculated to contain 247 mg/L (based on weight of sample before and after exposure) for a period of one hour. During the exposure, all animals showed eye irritation, salivation and marked anesthesia. Two hours after exposure, all animals had recovered. All rats appeared normal and gained weight during the 2-week observation period. No lesions attributable to test material exposure were observed upon gross pathological examination.

References for supporting data

Acute Toxicological Properties and Industrial Handling Hazards of 1,2-Dimethoxyethane. Dow Chemical USA, R&D Report August 25, 1983. TSCA Initial Submission (Final Report) With Cover Letter Dated 051492. NTIS/OTS0539769

Acute Dermal Toxicity

Type	**Acute Dermal Toxicity**
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4 (Aldrich Chemical Company)

Method

- Guideline: None specified
- GLP: No
- Year: 1983
- Species: Rabbit
- Strain: Not specified
- Route of administration: Dermal administration
- Doses: 1000 or 2000 mg/kg
- Sex: Female
- Exposure Period: Not specified
- Number of Animals/group: Four
- Vehicle: None

Remarks Field for Test Conditions

◊	Age at Study Initiation	Unknown
◊	Doses	1000 or 2000 mg/kg
◊	Post-dose observation period	14 Days

Results

- LD_{50}: 1000 mg/kg (approximately 2000 mg/kg)
- Number of deaths at each dose level:

Dose level	Deaths
1000	0/2
2000	1/2

Remarks Field for Results	Clinical Signs	Rabbits at the 1000 mg/kg level appeared healthy and gained weight during the 14-day observation period.

Conclusions

Remarks field

The dermal LD_{50} for female rabbits is >1000 mg/kg. Since one of two rabbits died at the 2000 mg/kg dose level, the LD_{50} may be in the range of 2000 mg/kg. Study was conducted by a well-known and experienced laboratory. The data and supporting study indicate that the test material has the ability to be absorbed through the skin.

Data Quality

- Reliability

Klimisch Code 2. Study reporting is considered reliable to address the test endpoint in light of confirmatory information from another study.

References

Acute Toxicological Properties and Industrial Handling Hazards of 1,2-Dimethoxyethane. Dow Chemical USA, R&D Report August 25, 1983. TSCA Initial Submission (Final Report) With Cover Letter Dated 051492. NTIS/OTS0539769

Other

This study is supported by a report that the dermal LD_{50} in guinea pigs for this material is between 5 and 10 ml/kg (1).

References for supporting data

1. Initial Submission: Letter From Dupont Chem To USEPA Regarding Toxicity Studies Of 1,2-Dimethoxyethane With Cover Letter Dated 10-15-92. EPA/OTS; Doc #88-920009666 NTIS/OTS0571323

Repeated Dose Toxicity,

Rat Thirteen-Week Drinking Water

Type	**Repeated Dose Toxicity, Thirteen-Week Drinking Water**
Test Substance	Surrogate 2-Methoxyethanol CAS 109-86-6
Method	
• Guideline	NTP Statement of Work
• GLP	Yes
• Year	1993
• Species	Rat
• Strain	Fisher 344
• Route of administration	Drinking Water
• Duration of Test	13 Weeks
• Doses	0, 750, 1500,3000, 4500 or 6000 ppm
• Sex	Male and Female
• Exposure Period	Continuous
• Frequency of Treatment	Daily
• Number of Animals/group	Ten of each sex
• Control Group and Treatment	Drinking water only
• Post-Exposure Observation Period	None for main group Stop group at 1500 and 3000 ppm, dosed 60 days, stopped 30 days
• Statistical Methods	◊ Standard NTP according to Statement of Work.

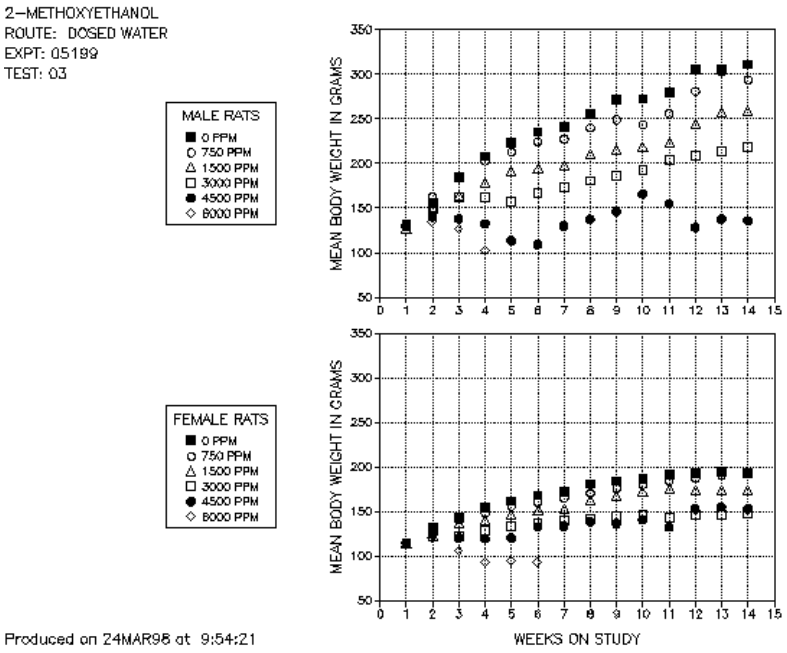
Remarks Field for Test Conditions	◊ Age at study initiation	About 6-7 weeks
	◊ Number of animals per Sex per dose	Ten
	◊ Measured Doses	70 to 800 mg/kg
	◊ Satellite groups	Stop group

	◊ Housing	Individually housed in stainless steel cages
	◊ Clinical observations performed and frequency	▪ Mortality and gross signs: Twice daily ▪ Abnormal signs: Daily ▪ Detailed physical examination: Twice weekly
	◊ Terminal observations	▪ Blood taken for hematology and clinical chemistry. ▪ Complete gross postmortem examination including external surfaces, all orifices, the cranial cavity, carcass, the external surface of the brain and spinal cord, the thoracic, abdominal and pelvic cavities and their viscera and the cervical tissues and organs were examined for all animals.
	◊ Histopathology	Complete for control and high-dose. Affected organs read down to NOAEL

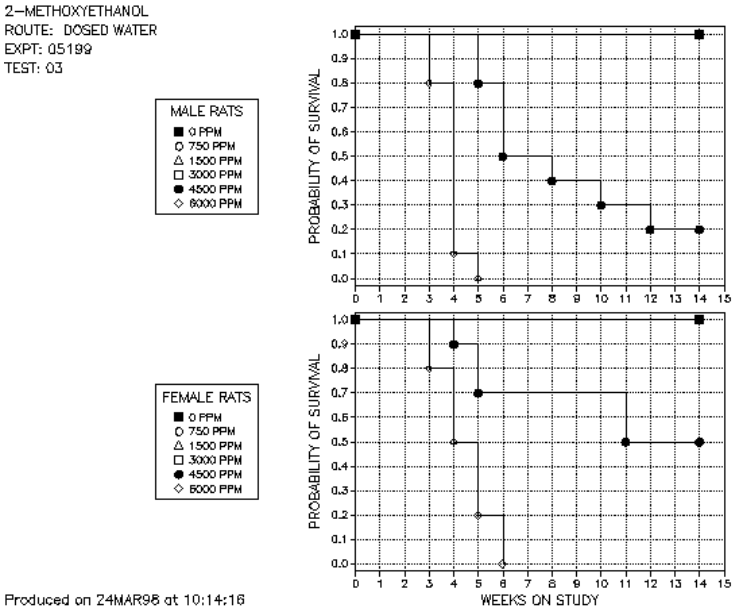
Results

• NOAEL	◊ ◊ A NOAEL was not reached. Testicular degeneration in males and decreased thymus weights in males and females occurred at the lowest concentration administered (750 ppm).
• LOEAL	◊ Males 750 ppm ◊ Females: 750 ppm
• Mortality	Chemically related mortality observed at 4500 and 6000 ppm in males and females.
• Toxic Responses	Dose-related reductions in body weight gains were reproted. Treatment-related histopathologic changes were observed in the testes, thymus, and hematopoietic tissues (spleen, bone marrow, and liver). A dose-related degeneration of the germinal epithelium in the seminiferous tubules of the testes was observed. In special stop-exposure studies in male rats in which administration of 2-ME was stopped after 60 days, marked degeneration of the seminiferous tubules was present in rats treated with 3000 ppm 2-ME, and mild to moderate degeneration was observed in rats treated with 1500 ppm.

◊ Body Weight Data



◊ Survival Data



Remarks Field for Results

◊ Hematology

Treatment for 13 weeks resulted in a progressive anemia associated with a cellular depletion of bone marrow and fibrosis of the splenic capsule.

◊ Necropsy findings	See above

Conclusions

Remarks field	Treatment was associated with dose-related testicular degeneration and reduction in thymus weights at the low dose. Higher doses also produced a progressive anemia.

Data Quality

● Reliability	Klimisch Code 1. Study design, conduct and reporting are considered reliable to address the test endpoint.

References	NTP Technical Report TOX-26. Toxicity Studies of Ethylene Glycol Ethers: 2-Methoxyethanol, 2-Ethoxyethanol, 2-Butoxyethanol (CAS Nos. 109-86-4, 110-80-5, 111-76-2) Administered in Drinking Water to F344/N Rats and B6C3F_1 Mice
Other	This study is supported by numerous other studies by the gavage, inhalation and dermal routes in various species also showing testicular degeneration and anemia. (See Hazardous Substance Data Base for a listing of studies)
References for supporting studies	

Repeated Dose Toxicity, Mouse Thirteen-Week Drinking Water

Type	**Repeated Dose Toxicity, Thirteen-Week Drinking Water**
Test Substance	Surrogate 2-Methoxyethanol CAS 109-86-6
Method	
• Guideline	NTP Statement of Work
• GLP	Yes
• Year	1993
• Species	Mouse
• Strain	B6C3F1
• Route of administration	Drinking Water
• Duration of Test	13 Weeks
• Doses	0, 2000, 4000, 6000, 8000 or 10000 ppm
• Sex	Male and Female
• Exposure Period	Continuous
• Frequency of Treatment	Daily
• Number of Animals/group	Ten of each sex
• Control Group and Treatment	Drinking water only
• Post-Exposure Observation Period	None for main group
• Statistical Methods	◊ Standard NTP according to Statement of Work.

Remarks Field for Test Conditions	◊ Age at study initiation	About 6-7 weeks
	◊ Number of animals per Sex per dose	Ten
	◊ Measured Doses	300 to 1800 mg/kg
	◊ Satellite groups	
	◊ Housing	Standard

◊	Clinical observations performed and frequency	▪ Mortality and gross signs: Twice daily ▪ Abnormal signs: Daily ▪ Detailed physical examination: Twice weekly
◊	Terminal observations	▪ Blood taken for hematology and clinical chemistry. ▪ Complete gross postmortem examination including external surfaces, all orifices, the cranial cavity, carcass, the external surface of the brain and spinal cord, the thoracic, abdominal and pelvic cavities and their viscera and the cervical tissues and organs were examined for all animals.
◊	Histopathology	Complete for control and high-dose. Affected organs read down to NOAEL

Results

- NOAEL

  For male mice the NOAEL for testicular degeneration and increased hematopoiesis in the spleen was 2000 ppm. A NOAEL was not reached for female mice since adrenal gland hypertrophy and increased hematopoiesis in the spleen occurred at the lowest concentration administered

- LOAEL

  ◊ Males 4000 ppm
  ◊ Females: 2000 ppm

- Mortality

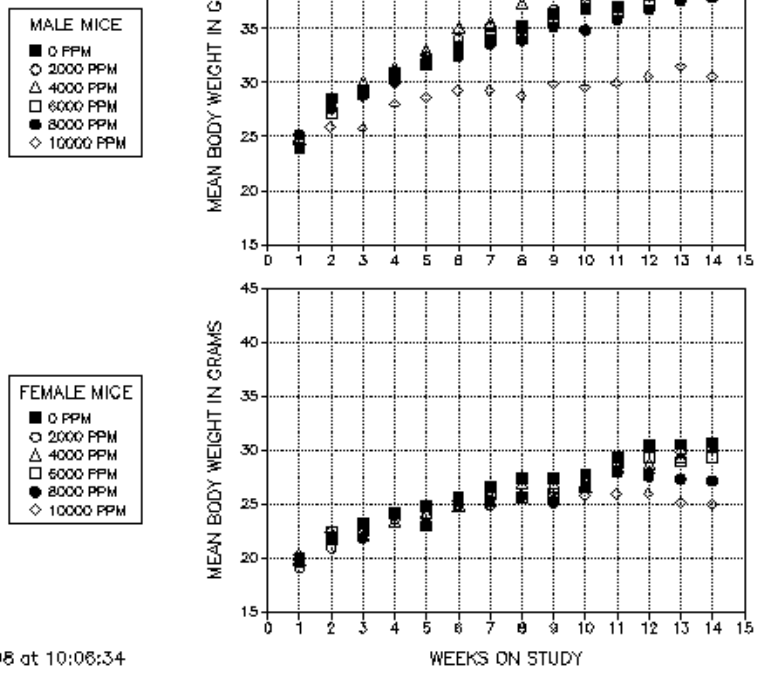
  No mortality was observed.

- Toxic Responses

  In mice, 2-ME had dose-related efects on the testes (4000 ppm and above), spleen, and adrenal gland (females only). A dose-related degeneration of the germinal epithelium in seminiferous tubules of the testes was observed. A dose-related increase in splenic hematopoiesis was more prominent. 2-ME caused a prominent lipid vacuolization of the X-zone of the adrenal gland in female mice.

◊ Body Weight Data

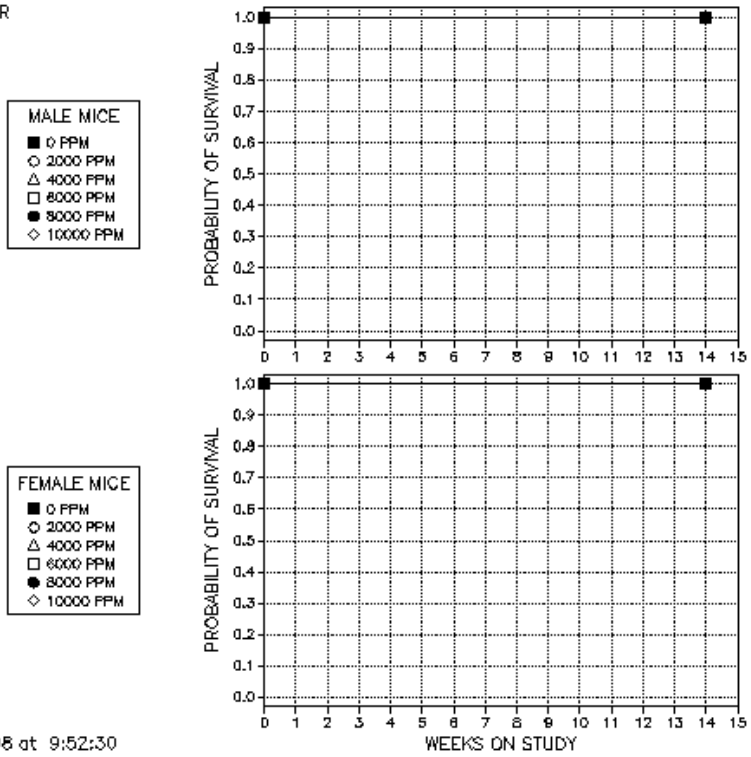
2-METHOXYETHANOL
ROUTE: DOSED WATER
EXPT: 05199
TEST: 07



Produced on 24MAR98 at 10:06:34

◊ Survival Data

2-METHOXYETHANOL
ROUTE: DOSED WATER
EXPT: 05199
TEST: 07



Produced on 24MAR98 at 9:52:30

Remarks Field for Results	◊ Hemat-ology	Treatment for 13 weeks resulted in a progressive anemia associated with a cellular depletion of bone marrow and fibrosis of the splenic capsule.
	◊ Necropsy findings	See above

Conclusions

Remarks field

Treatment was associated with dose-related testicular degeneration in males at 4000 ppm and above and adrenal gland hypertrophy in females even at the low dose. Higher doses also produced a progressive anemia.

Data Quality

- Reliability

Klimisch Code 1. Study design, conduct and reporting are considered reliable to address the test endpoint.

References

NTP Technical Report TOX-26. Toxicity Studies of Ethylene Glycol Ethers: 2-Methoxyethanol, 2-Ethoxyethanol, 2-Butoxyethanol (CAS Nos. 109-86-4, 110-80-5, 111-76-2) Administered in Drinking Water to F344/N Rats and B6C3F_1 Mice

Other

This study is supported by numerous other studies by the gavage, inhalation and dermal routes in various species also showing testicular degeneration and anemia. (See Hazardous Substance Data Base for a listing of studies)

References for supporting studies

Genetic Toxicology

Chinese Hamster Ovary Cell Mutation Test (HGPRT)

Type Chinese Hamster Ovary Cell Mutation Test (HGPRT)

Test Substance 1,2-Dimethoxyethane
CAS Number: 110-71-4
Greater than 99% pure

Method

- Guideline: None specified but protocol is accord with OECD476
- GLP: No
- System of Testing: Non-bacterial
- Year: 1983
- Species/Strain: Chinese Hamster Ovary Cells (CHO)
- Metabolic activation: Tested with and without liver S9 metabolic activation system.
- Concentrations tested: Without S-9: 4.0, 4.5, 5.0, 5.5 and 6.0 % v/v
  With S-9: 3.5, 4.0, 4.5, 5.0 and 5.5 % v/v
- Statistical Methods: Based on $p > 0.05$ in Student's t-test

Remarks Field for Test Conditions

- ◊ Quadruple plates for cytotoxicity and counting mutant colonies
- ◊ Solvent, direct addition of test substance without solvent
- ◊ Negative control, water and medium
- ◊ S9 produced from Aroclor 1254 induced Sprague-Dawley rats. S9 purchased from commercial source (Meloy Lab) a concentration of 4847 µg. S9 protein was added per 5 ml culture medium.
- ◊ Positive controls
  - Without activation - EMS
  - With activation - DMN

Results

- Result

Material was consistently inactive as a mutagenic agent for CHO cells in the presence or absence of metabolic activation at concentrations of test substance that included doses producing marked cytotoxic effects. No dose-related or significant effects were observed in any of the mutagenicity tests. Positive controls demonstrated the sensitivity of the test system.

- Cytotoxic Concentration

Conc.	Cytotoxicity Test Percent Survival (24 hours)	
(% v/v)	Without S-9	With S-9
3.5	ND	93.0
4.0	92.5	75.2
4.5	104.5	51.5
5.0	93.2	8.0
5.5	78.0	2.2
6.0	11.8	< 1
6.5	< 1	< 1

- Genotoxic Effects

No genotoxic activity under activation or non-activation conditions.

Remarks Field for Results

◊ Material was soluble in water
◊ Plating efficiency in the mutation test was better than predicted by the cytotoxicity test.
◊ Each of the quadruplicate plates showed similar numbers of colonies as other plates in that group and no plates were found contaminated.

Conclusions

Remarks field

◊ No genotoxic activity under non-activation conditions

◊ Study was well conducted, although there was no GLP certification the study appears to have been conducted using a GLP-quality protocol in a GLP compliant laboratory.

Data Quality

- Reliability

Klimisch Code 2. Reliable with restrictions. Study design, conduct and reporting are considered reliable to address the test endpoint although not conducted in accord with GLP standards.

References

1,2-Dimethoxyethane (Ethylene Glycol Dimethylether) *In Vitro* Mutagenesis Studies: 3-Test Battery. Final report with cover letter, NTIS/OTS0534903, Union Carbide, Bushy Run Research Center, 2/10/1983. Part 1

Sister Chromatid Exchange in Chinese Hamster Ovary Cells (SCE Test)

Type	Sister Chromatid Exchange in Chinese Hamster Ovary Cells (SCE Test)
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4 Greater than 99% pure

Method

- Guideline: None specified but protocol is accord with OECD479
- GLP: No
- System of Testing: Non-bacterial
- Year: 1983
- Species/Strain: Chinese Hamster Ovary Cells (CHO)
- Metabolic activation: Tested with and without liver S-9 metabolic activation system
- Concentrations tested: Without S-9: 2.0, 3.0 and 4.0 % v/v
With S-9: 3.0, 4.0 and 5.0 % v/v
- Statistical Methods: Data analyzed by Duncan's multiple range test by comparisons to the negative control.

Remarks Field for Test Conditions

- ◊ Duplicate cultures for cytotoxicity and SCE determination.
- ◊ S9 produced from Aroclor 1254 induced Sprague-Dawley rats. S9 purchased from commercial source (Litton a concentration of 600 µg. S9 protein was added per 5 ml culture medium.
- ◊ Solvent, direct addition of test substance without solvent
- ◊ Negative control, medium
- ◊ Positive controls
    - o Without activation – EMS
    - o With activation – DMN

Results

- Result

Active in production of SCE's in the absence and presence of S9 activation system.

- Cytotoxic Concentration

Conc. (% v/v)	Cytotoxicity Test Percent Survival (24 hours)	
	Without S-9	With S-9
3.5	ND	93.0
4.0	92.5	75.2
4.5	104.5	51.5
5.0	93.2	8.0
5.5	78.0	2.2
6.0	11.8	< 1
6.5	< 1	< 1

- Cytotoxicity continued

Mitotic Inhibitory Effects

Conc. (% v/v)	Percent Cells at Respective Mitotic Division					
	Without S-9			With S-9		
	First	Second	Third	First	Second	Third
2.0	1.9	98.1	0			
3.0	36.4	63.0	0	7.2	92.0	0
4.0	33.2	66.8	0	13.8	86.2	0
5.0	-	-	-	16.6	83.4	0
- Control	6.9	87.8	5.4	1.8	89.3	8.9
+ Control	43.2	56.8	0	7.4	92.6	0

- The decreasing percentage of cells in second and third division as the test concentration increased indicated cytotoxic inhibition of cell division in the cells tested with and without S-9 as compared to the negative controls. This finding verified that the tested concentrations were in an appropriate biologically effective range.

-

- Genotoxic Effects: Evidence of genotoxic activity under activation and non-activation conditions.

Remarks Field for Results

Results of SCE and Chromosome Aberration Examination

Conc. (% v/v)	SCE/cell		Percent Cells With Chromosome Aberrations	
	Without S9	With S9	Without S9	With S9
2.0	11.1*	-	0	-
3.0	10.3*	12.9*	0.9	7.4
4.0	11.7*	14.3*	1.3	6.9
5.0	-	14.4*	-	5.0
- Control	8.26	10.5	1.3	1.8
+ Control	23.48	43.3*	4.5	7.4

* Statistically significant

- Statistical significance not determined for chromosome aberrations since this test was not designed for quantitative determination of chromosome aberrations.

Conclusions

Remarks field: Material produced numerous indications of statistically significant effects on the frequency of SCE over the range of concentrations tested with and without addition of an active S9 metabolic system. A high number of cells were also observed with significant types of chromosomal aberrations suggesting that material was a clastogenic agent, especially in the presence of S9 activation.

- Reliability: Klimisch Code 2. Reliable with restrictions. Study design, conduct and reporting are considered reliable to address the test endpoint although not conducted in accord with GLP standards.

References

1,2-Dimethoxyethane (Ethylene Glycol Dimethylether) *In Vitro* Mutagenesis Studies: 3-Test Battery. Final report with cover letter, NTIS/OTS0534903, Union Carbide, Bushy Run Research Center, 2/10/1983. Part 2

***In Vitro* Unscheduled DNA Synthesis (UDS) Assay**

Type	*In Vitro* Unscheduled DNA Synthesis (UDS) Assay
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4 Greater than 99% pure
Method	
• Guideline	None specified but protocol was similar to OECD482
• GLP	No
• System of Testing	Non-bacterial
• Year	1983
• Species/Strain	Hepatocytes prepared from rats.
• Metabolic activation	None necessary
• Concentrations tested	0, 0.03, 0.1, 0.3. 1.0, 3.0 and 6.0 % v/v
• Statistical Methods	Data analyzed by Duncan's multiple range test by comparisons to the negative control. NQO data (a positive control) were analyzed using Student's t test due to its large variance.
Remarks Field for Test Conditions	◊ Duplicate samples except quadruplicate for controls. ◊ Solvent, direct addition of test substance without solvent ◊ Negative control, deionized water ◊ Positive controls o Activation control– 4-Nitroquinoline oxide o No activation control – DMBA

Results

- Result

Test material did not produce either statistically significant or dose-related increases in the amount of UDS activity.

- Cytotoxic Concentration

Conc. (% v/v)	Cytotoxicity Test Percent Survival (24 hours)	
	Without S-9	With S-9
3.5	ND	93.0
4.0	92.5	75.2
4.5	104.5	51.5
5.0	93.2	8.0
5.5	78.0	2.2
6.0	11.8	< 1
6.5	< 1	< 1

-

- Genotoxic Effects

No evidence of genotoxic activity.

Remarks Field for Results

Results of UDS as Measured by Tritiated-Thymidine Incorporation

Material	Conc.†	Radioactivity in nucleus		Radioactivity bound to DNA	
		DPM	% control	DPM	% control
Water - control	20	2101	100	1135	100
4-NQO + control	0.3	4929*	235	2805*	247
	1.0	5941*	283	3384	298

	3.0	3926*	187	2033*	179
DMBA + control	10	4904*	233	2245*	198
	30	1934	92	1086	96
	100	1459	69	762	67
Test Material	0.03	2507	119	1521	134
	0.1	2249	107	1247	109
	0.3	2869	137	1575	139
	1.0	1600	76	908	80
	3.0	2888	137	1591	140
	6.0	1040	49	602	53

† Test material in percent v/v, other materials in ug/ml

* Statistical significant difference from water control.

Conclusions

Remarks field

The maximum dose level was selected with consideration of the cytotoxicity data obtained with CHO cells which indicated that doses greater than 6.0% were extremely cytotoxic and caused complete lysis of treated cells. Typically, 0.5 % (by volume) is considered the usual maximum dose for testing; but dimethoxyethane had minimal cytotoxicity to CRO cells at concentrations up to 4.0% in the test with a metabolic activation system.

Analyses of DNA from aliquots of nuclei used for the thymidine uptake, were used as a second assessment of unscheduled incorporation of radioactive thymidine. For hepatocytes treated with 1,2-dimethoxyethane, none of the test concentrations induced levels of UDS that were statistically different from the concurrent solvent control. The highest dose (6 %) produced the same decrease in radioactive incorporation in DNA as in nuclei. This decrease is considered indicative of cytotoxicity to the hepatocytes at this dose level.

The protocol was conducted in accord with OECD 482 guidelines with regard to most experimental parameters. The number of replicates was fewer than recommended by the guideline and there was no independent repeat; however, more concentration levels were tested than typical and there was an independent radioactivity determination of nuclear DNA.

Data Quality

- Reliability

Klimisch Code 2. Reliable with restrictions. Study design, conduct and reporting are considered reliable to address the test endpoint although not conducted in accord with GLP standards.

References

1,2-Dimethoxyethane (Ethylene Glycol Dimethylether) *In Vitro* Mutagenesis Studies: 3-Test Battery. Final report with cover letter, NTIS/OTS0534903, Union Carbide, Bushy Run Research Center, 2/10/1983. Part 3

Reproductive Toxicology

Screening Study in Mice

Type	**Screening Study in Mice**
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4
Method	
• Guideline	None
• GLP	Yes
• Year	1983
• Species	Mouse
• Strain	CD-1 (Charles River)
• Route of administration	Oral Gavage
• Doses	0, 2000 mg/kg for pregnant females 0, 225, 450, 900, 1800 and 3600 mg/kg for rangefinding test
• Sex	Female
• Number of Animals/group	50 in pregnant 10 in rangefinding
• Vehicle	Water

Remarks Field for Test Conditions	◊	Age at Study Initiation	61 to 71 days
	◊	Doses for Pregnant	0, 2000 mg/kg/day (MTD)
	◊	Doses for Rangefinding	0, 225, 450, 900, 1800 and 3600 mg/kg
	◊	Dosing	Females only
	◊	Dosing Schedule	Seven days a week
	◊	Dosing Duration	Gestation day 7 to 14
	◊	Mating Parameters	Timed pregnant mice were obtained from Charles River Laboratory 2:1 females:males
	◊	Variations from OECD Guideline	There is no comparable OECD guideline for this screening study.
	◊	Weights	Maternal body weights were recoded on day 7 of gestation, day 18 of gestation and day 3 postpartum. Pups were weighed as a litter.

Conduct of study

Groups of 10 non-pregnant mice were dosed to determine the MTD for the developmental screening test (Target was dose causing 10% compound-related mortality). Mice were dosed daily for eight consecutive days in the rangefinding test. The MTD was determined from established weight criteria and 50 pregnant (sperm-plug positive) mice were dosed for eight consecutive days (7 to 14 of gestation) The individually- housed females were allowed to deliver pups. If no pups were delivered by day 23 of gestation, mice were sacrificed and non-gravid uteri were stained with sodium sulfide.

Results

- Result

No viable litters were produced from 49 pregnant mice dosed at 2000 mg/kg. Survival and mean body weight of non-pregnant rangefinding mice are given below

- Rangefinding Results

	Mean Body Weights of MTD Group (W grams) (Survival= S of 10)							
	Treatment Day 1		Treatment Day 8		Post-Treat Day 4		Post Treat Day 8	
Dose (mg/kg)	S	W	S	W	S	W	S	W
0	10	24.8	9	23.6	7	25.4	7	25.0
225	10	25.3	10	23.5	9	24.8	9	26.2
450	10	26.3	9	23.8	9	24.8	9	25.8
900	10	25.7	10	23.4	10	24.5	10	25.6
1800	10	25.3	9	25.0	10	26.2	1	27.1
3600	10	25.8	1	29.1	1	25.8	1	27.4

- Reproductive Results

Dose	2000 mg/kg
Litters Delivered	0/40 (9 mice died during the dosing phase)
NaS Positive	34
NaS Negative	3
Pup Parameters	No viable pups born

Remarks Field for Results	◊ Weights of pregnant animals	Sodium sulfide positive animals showed a mean weight loss (7%) between the start of dosing on day 8 of gestation and day 18. Controls showed a 13.3% increase in weight. The dose administered to pregnant mice exceeded the target of 10% mortality and maternal toxicity could have influenced the developmental results.

Conclusions

Remarks field	Pregnant mice receiving 2000 mg/kg/day of Monoglyme on days 8 to 14 of pregnancy did not deliver any viable pups. As the uteri of most of these were sodium sulfide positive, it is concluded that this material demonstrates significant embryotoxicity. at 2000 mg/kg in pregnant mice. Exceeding the target MTD may have increased the extent of the embryo-lethality.

Data Quality

• Reliability	Klimisch Code 1. Study design, conduct and reporting are considered reliable to address the test endpoint. Studies were done under the supervision of a quality assurance unit. Although there is no current EPA/OECD guidelines for this screen, it was conducted in accord with standard procedures at the time.

References

Screening of Priority Chemicals for Potential Reproductive Hazard. Final report for contract 210-81-6012. Prepared by Mesa Corporation, Orem Utah, sponsored by NIOHS Cincinnati Ohio, April 1983

Also published as: Schuler et al. results of Testing Fifteen Glycol Ethers in a Short-Term *In Vivo* Reproductive Assay. Environmental Health Perspectives 57:141-146 (1984)

Other

Developmental Toxicology

Developmental Toxicology, Oral

Type	**Developmental Toxicology, Oral, Teratology and Perinatal Effects**
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4 Material provided by NIOSH

Method

• Guideline	None
• GLP	No data
• Year	1991
• Species	Rat
• Strain	Sprague-Dawley, Harlan
• Route of administration	Oral gavage, as solution in water
• Doses	0, 30, 60, 120, 250 or 1000 mg/kg
• Sex	Female, pregnant
• Exposure Period	Days 8 to 18 of pregnancy
• Frequency of treatment	Daily
• Control Group	Water only
• Duration of test	About 14 days
• Statistical Methods	A computer-assisted assessment of the data was performed using RUMMAGE (Statistics Department, Brigham Young University), which utilizes a general linear model. For each parameter, overall tests of difference among the treatment groups were made using F tests. Statistical significance of differences in skeletal ossification (stain intensity), litter size, fetal and newborn weight, and mortality (average number of resorptions, day 19; average number of stillbirths) was determined using one-way analysis of variance. The significance of differences between pairs of means for all parameters tested was obtained using Student's *t* test. A weighted analysis of variance was utilized for mortality where the weight was the reciprocal of the number of resorptions (or stillbirths) since the variance in those measurements was proportional to their means. An analysis of the values obtained in the skeletal ossification study confirmed the legitimacy of using average stain ratings per litter as the experimental and statistical unit; a normal probability plot of the residuals demonstrated "normality" in these data

Remarks Field for Test Conditions	◊ Age at Study Initiation	No data, animals were virgins and weight was 200-250 grams at breeding.

◊	Number of animals per group	Group Number pregnant dams 0 28 30 18 60 23 120 6 250 8 500 6 1000 6 Dams from the 1, 30 and 60 mg/kg/day group were selected for sacrifice at gd 19 for teratological evaluation of pups.
◊	Vehicle	Deionized water
◊	Clinical Observation Performed and Frequency	Behavior and health observed at least daily. Body weights determined daily.
◊	Mating Procedures	Virgin females were mated 1:1 with males in suspended mating cages. The day of vaginal plug detection was defined as day-0 of gestation.
◊	Maternal Parameters Assessed During Study	Body weight, general health, implantations.
◊	Fetal Parameters Assessed During Study	Litter size, early deaths (incusing estimation of time) gross malformations, perinatal size, fetal body weight, skeletal examination

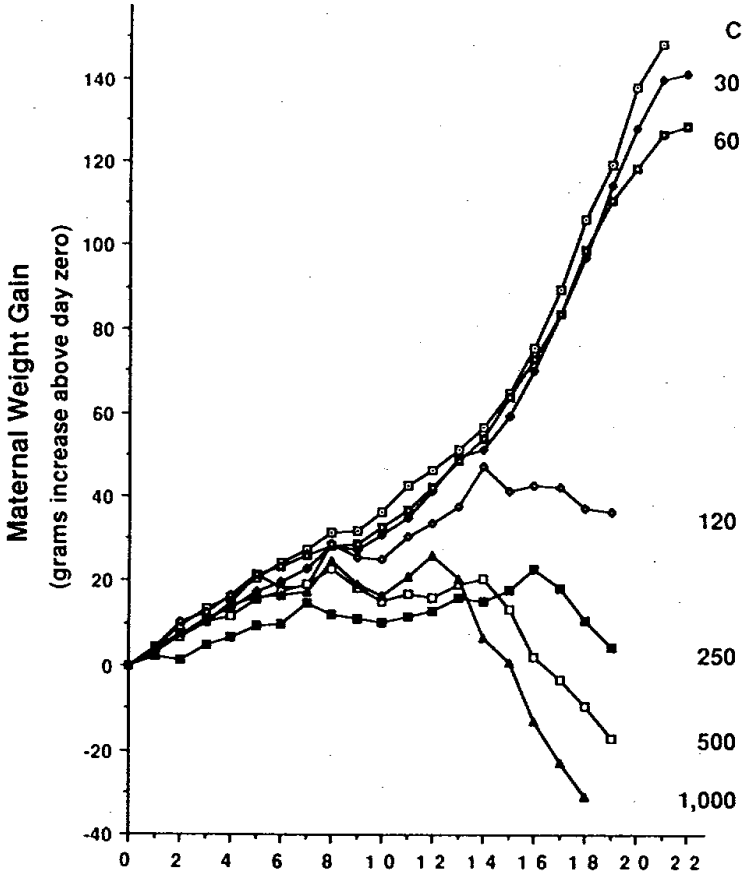
Results

• NOAEL & LOEL for Maternal Toxicity	NOAEL = not established, considered 60 mg/kg.day LOEL = 120 mg/kg/day body weight gain (partly due to early deaths)
• NOAEL & LOEL for Developmental Toxicity	NOAEL = < 30 mg/kg/day LOEL = 30 mg/kg/day retarded ossification
• Actual Doses Received	0, 30, 60, 120, 250 or 1000 mg/kg

- Maternal data

Body weights are shown in the graph.

Mortality @ 1000 mg/kg, 4/6 died (day 17-19)



- Gestational length was affected by treatment as shown below:

Treatment	Dose (mg/kg/day 8-18)	Number of litters	Gestational length Number litters each day		
			-21	21	21+
Water	-	16	1	15	0
Glyme	30	14	0	9	5
Glyme	60	15	0	3	12

Parturition was delayed by almost a full day at 60 mg/kg.

- Fetal data

◊ Cesarean Data

Cesarean data only collected for 0, 30 and 60 mg/kg groups, other dams were examined at time of early death (1000 mg/kg group) or at study termination.

Dose mg/kg	# litters	Average total implants	Mortality Live Average	%	Resorptions Average		%	Weight (g) Average /litter	
-	10	13.4 ± 1.6	13.0 ± 1.5	97	0.3	± 0.5	3	2.46 ±	0.56
30	7	13.1 ± 1.5	12.7 ± 1.3	97	0.4	± 1.3	3	2.46 ±	0.40
60	14	13.4 ± 2.6	11.2 ± 3.6	84	2.1	± 2.46	16	2.12 ±	0.43
120	6	14.0 ± 2.8	0		14.0	± 2.8`	100	-	
250	8	13.8 ± 3.2	0		13.8	± 3.2`	100	-	
500	6	14.8 ± 1.7	0		14.8	± 1.7	100	-	
1000	6	13.3 ± 2.3	0		13.3	± 2.3`	100	-	

◊ External and visceral effects

There was no indication of adverse effects to soft tissue.

◊ Major skeletal defects

The skeletal and soft tissue assays did not reveal any specific teratogenic defects in offspring exposed to 30 or 60 mg/kg/day. There was evidence, however, for generalized fetotoxicity. Of fetuses exposed at 60 mg/kg, 28% per litter exhibited substantial edema. Though much less frequent, the edema observed at the lower dose may also have been biologically significant; no control fetuses showed an effect.

In the skeletal assay, the stain rating of day 19 fetuses of the 60 mg/kg/day group was significantly reduced compared to the controls. This was a general observation, not restricted to specific bones. Such a result, indicative of less advanced bone ossification, is consistent with overall retardation of growth and development

- Fetotoxicity: Glyme administration was associated with significant fetotoxicity producing fetal edema and delayed ossification as shown in the table below

Dose (mg/kg/day) 8-18	Total number litters /fetuses	Edema Number affected litters	% Affected fetuses /litter	Total number litters/ fetuses	Retarded skeletal maturation Number affected litters	Average stain rating /litter
0	8/101	0	0	8/25	2	3.9
30	7/ 89	2	5.0			
60	10/ 35	6	28.4	10/28	8	2.5*
* = P < 0.05						

- Postnatal Data: Significant post-natal effects were observed as manifested by the high incidence of stillbirths and poor survival of 60 mg/kg group pups with only one remaining alive on day 1. The dams were reported not to care for the young and no milk was found in pups stomachs.

Dose group	# litters	Total pups per litter	Live Average Births per Litter	Mortality Stillborn Average	Live Average day 1	Weight Birth (g)	Weight Day 1 (g)
0	16	13.2 ± 2.2	13.0 ± 2.2	0.3 ±0.4	12.3 ± 2.8	6.34 ± 0.3	6.37 ± 0.43
30	14	11.9 ± 3.4	10.9 ± 3.0	1.7 ± 3.06	10.6 ± 3.4	6.01 ± 0.4	6.60 ± 0.90
60	15	9.5 ± 2.3`	4.8 ± 4.2	4.7 ± 2.8	0.2 ± 0.6	5.89 ± 0.76	5.49 ± 0.30

- ◊

Remarks for Results

Dose levels of 1000, 500, 250, and 120 mg/kg/day produced 100% resorptions. At the three highest concentrations, the necrotic masses were uniformly small, suggesting early embryonic death soon after treatment was initiated. In contrast, resorptions were not uniform in the 120 mg/kg/day groups. These dams carried fetuses varying in size from 1.5 to 2.0 cm in length, having survived for somewhat longer times. These observations are consistent with the dose-dependent reduction by Glyme in maternal weight gain during the second phase of the profile. While fetomortality was not elevated in the 30 mg/kg/day group, those dosed at 60 mg/kg/day suffered a 7-fold increase in the average number of resorptions per litter.

In the 60 mg/kg/day group, fewer than 1 pup per litter survived compared to 12.3 in controls. These pups did not receive maternal care (none were observed to have milk in the stomach), and none survived beyond day 1. The number of live pups at birth was reduced by an average of 2 pups at a dose of 30 mg/kg/day, but there was no significant loss in these litters during the first 24 h. The pups in the 60 mg/kg/day dosage group were 7% smaller than controls. This is a minimum difference, however, because these pups were actually developmentally older than controls due to a one-day delay in the onset of parturition.

The lowest dose employed, 30 mg/kg/day, appeared to be very close to the toxic threshold; there were few apparent prenatal effects at this level, and only a modest increase in the number dead at birth.

Conclusions

Remarks field

Administration of test material was associated with a clear dose-response related maternal and fetal toxicity. At the high doses (120 mg/kg and above) there was complete early fetal death and possible maternal toxicity. The lower doses were associated with fetotoxicity including stillbirths and reduced body weight. Major external malformations were not reported. There was a delay in parturition of almost a full day at the 60 mg/kg dose. A NOEL for developmental effects was not identified. The maternal NOEL was at least 30 mg/kg but could have been higher. It is not known if the lack of pup care provided by dams in the 60 mg/kg dose represents a maternal toxicity. This material causes developmental effects at levels below maternal toxicity.

Data Quality

- Reliability

Klimisch Code 2. Reliable with restriction, study not conducted according to GLP standards; however procedure is well documented and published in a peer reviewed jounal.

References

Leonhardt, DE, Coleman, L and W Bradshaw. Perinatal Toxicity of Ethylene Glycol Dimethyl Ether in the Rat. Reproductive Toxicology 5:157-162 (1991).

Other	Supporting data comes from a screening study in mice where pregnant mice receiving 2000 mg/kg/day of glyme on days 8 to 14 of pregnancy did not deliver any viable pups. As the uteri of most of these were sodium sulfide positive, it is concluded that this material demonstrates significant embryotoxicity. at 2000 mg/kg in pregnant mice. Exceeding the target MTD may have increased the extent of the embryo-lethality.
References for supporting studies	Screening of Priority Chemicals for Potential Reproductive Hazard. Final report for contract 210-81-6012. Prepared by Mesa Corporation, Orem Utah, sponsored by NIOHS Cincinnati Ohio, April 1983

Developmental Toxicology, Oral, Mouse

Type	**Developmental Toxicology, Oral**
Test Substance	1,2-Dimethoxyethane CAS Number: 110-71-4
Method	
• Guideline	None
• GLP	No data
• Year	1980
• Species	Mouse
• Strain	CRJ:CD-1 (I.C.R.)
• Route of administration	Oral gavage, as a solution in water
• Doses	0, 250, 350, 490 mg/kg
• Sex	Female, pregnant
• Exposure Period	Days 7 to 10 of pregnancy
• Frequency of treatment	Daily
• Control Group	Water only
• Duration of test	11 days
• Statistical Methods	Chi suared tests were used to compare test groups to controls for survival and numbers of affected fetus. Student's t-Test.

Remarks Field for Test Conditions

◊	Age at Study Initiation	No data
◊	Number of animals per group	Unbalanced design 0 mg/kg 23 250 mg/kg 23 350 mg/kg 23 490 mg/kg 28
◊	Vehicle	Distilled water
◊	Clinical Observation Performed and Frequency	Behavior and health observed Body weights determined on days 0, 3, 7, 10, 13, 15 and 18 of gestation.
◊	Maternal Parameters Assessed During Study	Body weight, clinical signs, ,number of implantation sites

◊	Fetal Parameters Assessed During Study	Litter size, live -dead embryos, placental weight, gross malformations,, fetal body weight, external malformations, skeletal examination
◊	Organs Examined at Necropsy	Viscera examined
◊	Dose Selection	No data.

Results

- NOAEL & LOEL for Maternal Toxicity

  NOAEL = 490 mg/kg based on body weight and clinical signs

  LOEL >490 mg/kg body weight gain

- NOAEL & LOEL for Developmental Toxicity

  NOAEL = 250 mg/kg malformations

  LOEL = 250 mg/kg/day fetal weights, retarded ossification

-

- Maternal data

  Body weight gain was not affected by dosage nor were there any obvious physiological change.

- Fetal data

  ◊ Cesarean Data

  Litter size was comparable in all groups, the incidence of fetal death was significantly increased at 490 mg/kg

  Fetal weights were significantly reduced in all does groups as compared to control, and a clear dose-response relationship was observed.

  Placental weight was significantly lower than control at 350 and 490 mg/kg.

  ◊ External and visceral effects

  See table

  ◊ Major skeletal defects

  Dose related effects were reported.

  Cervical vertebrae malformations (control to high dose)

  0, 25% ,34%, 46%

  vertebral synostosis

  0%, 15%, 45%, 58%

  rib fusions

  0.4% 21%,54%, 71%

- Fetal data
  - ◊ Malformations

External Malformations	Dose Group			
Parameter	0	250	350	490
Dams	23	23	23*	28*
Viable fetuses	272	291	293	323*
Exencepaly	0/272	1/291	11/293	28/323*
Eye open	0/272	0/291	2/293	16/323
Defective tail	0/272	0/291	2/293	14/323
Abdominal hernia	0/272	0/291	9/293	3/323
Cleft palate	0/272	0/291	0/293	1/323
Total malformations	0/272	1/291	15/293	62/323
Percent total	0%	0.3%	5.1%	19.2%

-

Remarks Field for Results: There is a clear dose-response relationship for malformations and embryo toxicity. Maternal data are scant and information on relevant parameters for gauging maternal toxicity, such as feed consumption, are not available.

Conclusions

Remarks field: There is a clear dose-response relationship for malformations and embryo toxicity. Administration of the test material was associated with increases in external and skeletal malformations. The low dose (250 mg/kg) appears to be a NOEL for external malformations but significant skeletal effects persist at the low dose. The low dose also appears to be associated with reduced fetal weight. The findings are clouded slightly by the lack of data demonstrating absence of maternal toxicity.

Data Quality

- Reliability: Klimisch Code 2. . Reliable with restrictions

References

Uemura, K. The Teratogenic Effects of Ethylene Glycol Dimethyl Ether on Mouse. Acta Obst. Gynaec. Jpn. 32:113-121 (1980)

Other

References for supporting studies